

Next-Generation Foods and CRISPR Engineering

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Big problems require big solutions. Grand challenges oftentimes will need grand technologies. We need to have the ability to deploy amazing disruptive technologies efficiently, at speed and at scale, to address some of the challenges aligned before us.

Think of a growing world population at a time where we need to feed it. Think the speed at which we need to alleviate, address and mitigate climate change. We need disruptive technologies that enable us to truly address those grand challenges. This is where team science comes in.

As scientists, our job is really to translate our scientific knowledge into useful, deployable technologies that we can then apply, hopefully, to develop products. It used to be hard to turn science into technology, into applications, and into products. But in some ways, this is the easy part. We need to be able to develop products that people accept, people endorse, people condone, people understand, people relate to. And one of the challenges of scientists is not just to turn science into technology, and apply those technologies to generate products, but also convince society, convince consumers, convince patients, convince regulators and governments, that those products are going to change their lives for the better.

Enter CRISPR-fueled genome editing. This is one of the most disruptive, momentous, powerful, promising technologies of the past generation. In just 10 years, just one decade of research and science, CRISPR-based genome editing, our ability to use CRISPR molecular machines to change, decode, rewrite and edit the DNA sequence of virtually any organism on planet Earth has been revolutionized. Just 10 years, extremely fast.

We now have a technology which has been, in many ways, democratized — 200,000 shipments of those molecular scalpels have been spread out and delivered to over 50,000 individuals, distributed across the world in over 100 countries. They've written and published over 20,000 studies that document the ability of this amazing disruptive technology to enable the average geneticist to rewrite the DNA of virtually any organism you can think of across the tree of life. From small, simple elemental viruses to bacteria. But also applicable to plants. Also applicable to crops, also applicable to mammals, and fish and large things like trees.

In just a decade of CRISPR research, this army of scientists spread throughout the world has had the ability to develop a whole compelling molecular toolbox that enables us to rewrite genomes. And this is what genome editing is. It's a fairly simple concept much like an editor editing text, a geneticist will edit the text of DNA. So just over the past 10 years, scientists have been able to develop a fairly sophisticated, very powerful molecular toolbox that enables scientists to use those tools to tinker, to change, to alter, to rewrite the DNA sequence of virtually any organism on planet Earth you can think of.

We can use those molecular tools to change the genome, change the transcriptome, change the epigenome, essentially change the series of letters that constitute our DNA code. But also control their

level of transcription. Are they transcribed and expressed heavily? Are they loud? Is the light turned on, or are they very quiet and turned off or turned down?

So an army of scientists now equipped with an amazing molecular toolbox has the ability to manipulate virtually, at will, programmably, the genomes of any species across the tree of life. And this has been done already in a number of examples. You can think of a CRISPR zoo whereby people in research labs have the ability to use those molecular tools to manipulate the genomes of model organisms or simple organisms. Think viruses, think bacteria, think yeast and fungi, or organisms that we use in a lab setting to model behavior, model development, model disease.

Things like mosquitoes, or worms or fish. Obviously, rats and mice, non-humanoid chimps, simple plants. But already outside of the academic world, outside of university settings, outside of fundamental research, this technology's already been deployed in the real world. Think about food. Think about ag. Think about forestry. Think about husbandry. Think about farming. Whether it's a crop – soy, wheat, rice, corn. Whether it's a food or a vegetable. Think mushrooms, or tomatoes. Whether it's livestock – think of poultry, think of swine and pigs. Think of cattle and cows, but it can also be seafood, shrimp, fish, on, and on, and on. The CRISPR zoo at large. Let your imagination fuel and take you to places where there's no boundaries whatsoever.

But beyond food and agriculture, already CRISPR has made it to the world of medicine, to the world of therapies, to the clinic. There's already people in the U.S. who have been dosed safely, and with efficacy, super clinical efficacy, with CRISPR-based gene therapies to address and correct typos in their genomes – mistakes in their DNA sequences – to address and alleviate genetic disease.

This is an extremely powerful technology that is changing our world in real time. But however promising, however compelling, however intriguing, however valuable, and compelling medical applications may be, some like me would argue that a lot of the benefits may actually lie in molecular breeding for the food supply chain.

Again, crops that we use to feed the world at a time where the population is growing concerningly fast. Those crops, can we use CRISPR-based molecular breeding and genome editing to literally breed at speed and at scale, more sustainable, higher yield, more safe, more efficient, more nutritious crops, more nutritious tomatoes, non-browning mushrooms, non-edible items like hemp or cotton? Besides plants, we can obviously use CRISPR-based generating technologies to alter and enhance microorganisms that we use across the food supply chain to feed ourselves, through fermentation processes we've actually used unbeknownst to us for millennia, as part of our culture, our idiosyncratic food supply. Think of all the fermented foods that hinge on bacteria, or yeast, and/or fungi. Think of yogurt, beer and champagne, all fermented vegetables.

But, of course, protein sources are very important to us. As a species, we like to eat meat. We can use CRISPR to edit cattle, dairy or not. We can use CRISPR to breed swine, think of a leaner bacon, or leaner poultry, leaner chicken. We can also enhance traits that are important for health, cattle on the farm that is more resistant to disease, infectious disease, bacterial disease, viral diseases, and on, and on, and on, and on.

And, of course, if you want to scale this up, think of trees, fruit trees, nut trees. But you can even go beyond just food-related forestry. We can talk about forestry at large, at a time where challenges are not just limited to feeding a growing population, but also addressing climate change. Not just a more

sustainable farm, but a more sustainable forest, where we can make trees more efficient, more reliable at capturing carbon, more resistant to pest and disease, viruses, fungi, insects, on, and on, and on.

And as a matter of fact, a lot of people are aware of an economic opportunity to use CRISPR as a game-changer for the world, in terms of sustainable agriculture at a time of inclusivity, at a time of equity, at a time of globalization, or food supply chain, at a time of water usage shortcomings and challenges. At a time where food security is important, at the individual level, at the local level, at the geopolitical context level, across nations and continents. And of course we need to have better and more sustainable food supply chains. More nutritious, more healthy, more efficient, more affordable, more accessible.

And think about numbers. We're talking about in the next 10 years, CRISPR-based genome editing being implemented at speed and at scale in up to 15% of all the farms that are comprised throughout the world. This number means one hundred million farms in the next seven years will plant genome edited crops. This will help us enhance our food production by at least 5%. This will enable us to, at speed and at scale, address sustainability, disease, water efficiency, to supply the local supply of food, local access. This will also enable us to enhance not just disease traits, not just yield, but also the chemical composition, the biochemical composition, the nutritional attributes of those crops.

We can now think of enhancing the nutrition profile of those crops to address malnutrition. That means that within the next seven years, the long Ph.D. cycle, so to speak, we could use and deploy CRISPR-based genome editing to address up to 5% of malnutrition. And this is just the beginning.

We are at the end of the beginning of the CRISPR-fueled genome editing revolution. It's interesting, it's intriguing, it's promising, and it's exciting. But with great applications often time come great implications for society. It's not just what can we do, but what should we do? Sometimes it's what should we not do?

As a matter of fact, it's not just scientists who have opinions. It's key opinion leaders, thought leaders throughout the world. Think of the Pope at the Vatican hosting a couple of hundred scientists dedicating their lives and to using CRISPR, and genome editing to develop gene therapies to address human health and disease, genetic disease.

His Holiness, the Pope, has an opinion on genome editing. We have a duty to care. And a duty to cure – quote, unquote.

If we have technologies and the ability to alleviate human pain and suffering, we have a duty to care and a duty to cure. If we have the ability to use CRISPR to correct genetic disease in patients afflicted by painful, sometimes terminal disease, do we not have a moral obligation to grant them access to that technology? If they're willing to do it, or if they're asking to do it, are we not obliged, if we can do it, to address their disease?

But what if some people are uncomfortable with our ability to change our DNA code, if it makes people uncomfortable, should they decide who can or who cannot change their DNA, or change their child's DNA, maybe their unborn child's DNA. And is DNA at the core of our nature, is it who we are? At our very core of human nature are we our DNA? Or is it the individual?

And who should decide whether or not somebody gets the right to change their DNA? Does the Pope's opinion matter more than mine or yours? Does the opinion of the patient matter more than the opinion

of their parent or vice versa? Depending on the age, depending on the jurisdiction, depending on the cultural context in which those decisions occur, I ask the question: whose opinions matter the most?

So it's not just the science and the technology, not just the applications, but the implications. The ethical and societal implications of our ability to responsibly or not deploy those very powerful disruptive technologies. We have to know when, we have to know how, we have to know if we should or not deploy that amazing molecular toolbox to change the genomes of virtually any organism on planet Earth.

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